Musical interlude

The Double Talking Helix Blues
Joel Herskowitz

The song below is a talking blues in the style of Woody Guthrie, written by Joel Herskowitz, a pediatric neurologist working in Boston.

The song is also available on tape, sung by Joel and his brother Ira, a yeast geneticist at the University of California, San Francisco, from Cold Spring Harbor Laboratory Press, 10 Skyline Drive, Plainview, NY 11803, USA. We reproduce it with the kind permission of the author.

Well, I once saw in an Addams cartoon
a Martian sittin' in a waitin' room.
It was late at night in the maternity ward,
A nurse appeared as she opened the door–
"Congratulations," she said "it's a baby!"

Well, the point of this story, I'll tell you now,
did you ever sit down and think about how
it is that every time a baby's born
it's a baby – not a rabbit or an ear of corn?

Well, it just so happens that inside everyone
are tiny plans that tell how the job's to be done;
They're worth more to you than the family jewels.
They're stored in the form of molecules.
Like everything else I guess.
Only different, and kind of special.

Now floatin' around in each one of your cells
is a nucleus, and you know what else –
tucked inside every one of these are chromosomes
that hold the keys
to the questions we asked:
'bout how humans beget humans.

Now these threadlike chromosomes contain
a groovy little substance that we're gonna name;
It's a macromolecule, as they say.
It's mighty fine stuff – called DNA.
That's "deoxyribonucleic acid"
For those of you out there with
expanding minds.

Now this DNA consists of a chain
of sugar and phosphate over and over again.
But just a minute's thought, and you'll see
there's no hope
for such a simple molecule to contain all the dope
to get the human show on the road,
that is, and into high gear.

Well, each of the sugars in the backbone
has a ring-shaped base 'tached to it all its own,
There's only four in a human bein':
Adenine, guanine, cytosine and thymine.
They make up an alphabet of four letters
– A, G, C, T.
Wouldn't want to write a novel with four
letters.
Think I'll write a human being instead.

Well, there's one important fact we've let slip by.
It earned three men the Nobel Prize.
It has to do with three-dimensional conformation,
and how it relates to information.

You see, DNA consists of two strands
joined together by the bases holdin' hands
in the form of hydrogen bonds, that is.
Any questions 'bout this?
The whole molecule forms a double helix –
A spiral staircase arrangement
with the nucleotide bases represented by
the steps.
Hope all this isn't too steep for you!

Now these bases join in a special way –
C with G and T with A.
The reason for that's not too complex.
I suggest you read about it in your text.
You know the book.
Some of you may even have bought it.

Now some time before a cell divides
an unknown factor in the cell decides
it's time to copy the DNA
so the new cell will know the way
to survive and do what it has to do –
A lot like us.

Hence, the double helices unzip,
and nucleotides in the neighborhood slip
into place next to their proper mates.
I think you see what this creates –
Two daughter macromolecules
identical to the parent.

So we see that every time a cell arises
there are not going to be too many surprises
because of this little template scheme,
this biological Xerox machine.

And when human parents make their contribution
to a baby-to-be's constitution –
Since their chromosomes are human,
we presume,
it's no shock that the baby is, too.

Well, I guess that brings us to the end of our tune
which began with a Martian in the waitin' room.
If you have any questions `bout something
you missed,
please see me. All class dismissed.

Gazetteer

Proceedings of the National Academy of Sciences, USA

What is it famous for? Being by far the most erratic of the journals that publish research papers in biology. A *PNAS* paper may be in the top 5% of papers in its field or the bottom 20%.

How did it start? The National Academy of Sciences was founded in 1863, and the journal started in a half-hearted way in 1877 (publishing roughly once a decade). Regular production began in 1915, and it became fortnightly in 1993

Why is its decision-making so erratic? The journal operates on what is, in effect, an honour system. Papers from National Academy members are accepted simply on their assurance that a 'knowledgeable colleague who is not a co-author' has reviewed the paper. Academy members also act as *ad hoc* editors for papers from other labs; all the editorial office asks is that they obtain two favourable reviews on the manuscript. A surprising number of Academy members take the journal very seriously and publish excellent papers there, but inevitably some are less scrupulous. The Editorial board does subject communicated papers to some further scrutiny, but this gentle probing rarely leads to outright rejection of papers.

How do I get my paper published in* PNAS *if I don't know an Academy member? Until this year, there was no way. But in January 1996, *PNAS* introduced a new system, known as 'track II', in which non-members can send their papers directly to the editorial office. The office then undertakes to identify a National Academy member who can act as the sponsor, select referees, and accept

or reject the paper. The author doesn't know which Academy member is handling the paper unless it is accepted. To make room for the extra papers to be submitted via track II, *PNAS* has reduced the number of papers a member is allowed to communicate to the journal annually from six to four.

Does the new system work? Those who have tried it say that there are many frustrating teething problems. Apparently one problem is that the Academy members are under no obligation to handle manuscripts when asked, so the editorial office may take weeks to identify a member who is willing and able to serve. Another problem is that, because the Academy member handling the manuscript is in effect one of the referees, the author cannot contact the person handling the manuscript directly to ask for a decision.

How do I find an Academy member? The journal's policy for publicizing the list of potential communicating members has changed over the years. For most of the 1980s, no list was published. Now the journal publishes a list of current members in the first issue of the journal each year; the list is also available on the internet (www.nas.edu/nas/member). But the truly crucial information — which members haven't used up their annual quota of submissions yet — is still very hard to discover, although lists of new members are published in the journal immediately after election.

Have there been any other changes since 1915? Recent changes include, in 1994, adding reviews and mini-reviews (Commentaries), which focus on papers published in *PNAS*. In 1995, the cover design was changed from plain grey (to provide 'aesthetic refreshment'); it now shows images taken from the fabric and contents of the National Academy of Sciences building in Washington, D.C.

The spider's web

Structural biology

Structural biologists are among the most computer-literate biologists and lead the way in use of the internet. This month, a few of the best tools are highlighted; URL links for all sites and programs listed in italics can be found with the electronic version of this article, available free of charge on *http://www.BioMedNet.com/cbiology/spider.htm*

Databases

The key web resource for structural biology is the *Brookhaven Protein Data Bank* (PDB). As of May 1996, it contained 4 113 atomic coordinate files, representing protein structures obtained by X-ray crystallography or nuclear magnetic resonance (NMR). Thanks to the extensive cross-linking of databases on the web, PDB files can now be searched many ways. The National Center for Bioinformatics' *Entrez* and the European Bioinformatics Institute's *Sequence Retrieval System* (see *Curr Biol* **6**:4) both include the PDB in their searches, but to be sure of getting the latest files, search the PDB directly.

Similarity searching

Although less straightforward than comparing primary sequences, computing a similarity score for two sets of atomic coordinates is possible. Most techniques simplify the problem by breaking the protein structure down into secondary structural units such as helices, loops and sheets, and comparing the arrangement of these units in different proteins.

Entrez makes available the results of an exhaustive comparison of all the structures in the PDB against each other, while *SARF* at the *Laboratory of Mathematical Biology* allows you to take a novel structure in PDB format and compare it against the rest of the database. *MOOSE* lets you retrieve structures from the PDB that match a specific structural motif specified in terms of secondary structural units such as 'helix–turn–helix'.

Structure prediction

Protein structure prediction is an evolving and imperfect process. Several web tools let you predict three-dimensional structure for a given primary sequence; a good listing of these is available at the *Centre for Protein Engineering*'s site. New tools are continuously becoming available, so the best way to keep up is to use an internet search, at a site such as *Alta Vista*.

Structure prediction can only be properly assessed by application to new and unpublished data, so there are several competitions with the goal of predicting the structure of a new protein from its primary sequence. Details of some of these, and abstracts describing the techniques used, are available from the *Centre for Advanced Research in Biotechnology* site.

Visualization

Sites such as *Molecules R US* and *Structural Classification of Proteins* let you select a protein from the PDB, choose an orientation, a colouring system, and a method of rendering — ribbons, space-filling or ball-and-stick — and then download a full colour image of the chosen protein. These sites use the programs *RASMOL* or *RASTER3D* to create their images. If you have the computing power, you can also download *RASMOL*.

Another popular method for visualization is the kinemage, viewed and rotated using the program *MAGE*, which represents a structure schematically. Some of the tools described here create kinemages automatically from the PDB file. The *Macromolecular Structures* database published by *Current Biology Ltd* offers kinemages which have been annotated by hand, and several journals including *Structure* and *Protein Science* now include kinemages as electronic supplements to articles.

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